

REMARKS

Applicants respectfully request reconsideration of the present application in view of the reasons that follow.

Claims 21-54 are pending.

I. Claim Rejections – 35 U.S.C. § 112, First Paragraph

Claims 21-54 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking enablement. According to the Examiner, the specification is enabling for “the mice taught in the specification.” Office Action at 5. However, the Examiner alleges that the full-scope of the claims is not enabled. Applicants respectfully traverse this ground of rejection.

As discussed below, the evidence and explanation of record establishes that one of ordinary skill in the art could practice the full scope of the claimed invention using only routine experimentation.

A. Enablement does not require the transgenic animal exhibit any particular phenotype

The Examiner states that “the issue at hand is: how does an artisan predictably identify any non-human transgenic animal comprising the tet system such that an artisan can use the transgenic non-human animal.” Office Action at 7. In other words, the Examiner alleges that the phenotypes of the transgenic animals are unpredictable and that the use of these transgenic animals would constitute undue experimentation based on this unpredictability. *See* Office Action at 7-11.

However, the enablement of the claimed invention should be based on the claim language and not on the nature of “phenotypes.” The claims state that the transcription of the gene of interest occurs “**at detectable levels.**” Thus, the claims do not require the transgenic animal exhibit a particular “phenotype.”

One skilled in the art would know how to use the claimed transgenic animal. For example, the claimed transgenic animal that transcribes a gene of interest “at detectable levels” could be used to produce a therapeutic protein encoded by the gene of interest. Application at page 50, lines 17-35. Other uses of the claimed transgenic animals would be immediately apparent to one of skill in the art. Indeed, the specification contains an entire section devoted to uses of the technology. Application at page 42, lines 10 – page 51, lines 32. Thus, the specification discloses multiple uses of the claimed invention.

B. The state of the art at the time of the invention shows that transgenic animals were produced using established methods without undue experimentation

The Examiner advances two primary arguments in support of the conclusion that the claims are not fully enabled. First, the Examiner alleges that “[t]here is unpredictability with regards as to where the transgene integrates in the genome and how many copies of the transgene integrate into the genome.” Office Action at 7. Second, the Examiner alleges that “integration of a transgene into an alternative species of animal may result in widely different phenotypic responses.” *Id.*

However, one of skill in the art would recognize and understand the potential issues associated with positional effects and variations between different species of animals. Accordingly, one of skill in the art could routinely screen litters of transgenic animals to identify such issues. Thus, positional effects and variations between different species would not render the claimed invention unpredictable because routine screening would be employed. Such routine screening does not constitute undue experimentation, even if the screening is time consuming. *See* MPEP 2164.01.

The state of the art supports Applicants’ position that making the claimed invention was routine at the time of filing based on the teachings of the specification. For example, the following references demonstrate the routine production of transgenic animals comprising gene expression systems resulting in detectable expression of a gene of interest:

- (a) Bello *et al.*, DEV. 125:2193-2202 (1998), describes the use of the Tet gene expression control systems in *Drosophila* (Exhibit A);
- (b) Bieschke *et al.*, MOL. GEN. GENET. 258:571-579 (1998), describes transgenic flies comprising the reverse Tet gene expression system to control transcription of *tet*-operator linked *lacZ* (Exhibit B);
- (c) Melfi *et al.*, J. MOL. BIOL. 304(5):753-763 (2001), describes the use of the Tet gene expression control systems in sea urchins to control expression of *sns* fragment (Exhibit C);
- (d) Ridgway *et al.*, EXP. CELL RES. 256(2):392 (2000), describes the effectiveness of the Tet gene expression system in *Xenopus* (Exhibit D);
- (e) Schultze *et al.*, NATURE BIOTECHNOLOGY, 14(4):499-503 (1996), describes production of transgenic organisms using Tet-regulated gene expression (Exhibit E);
- (f) St. Onge *et al.*, NUCLEIC ACIDS RES., 24(19):3875-77 (1996), describes production of transgenic mice, which express the Cre gene under the control of tetracycline repressor (tetR) and the acidic domain of the herpes simplex viral protein 16 (VP16) (Exhibit F);
- (g) Kistner *et al.*, PROC. NAT'L ACAD. SCI., 93(20):10933-38 (1996), describes the use of tet-regulatory systems in mice (Exhibit G); and
- (h) Weinmann *et al.*, PLANT J., 5(4):559-69 (1994), describes production of transgenic plants with tet-regulated genes (Exhibit H).

These references demonstrate the routine production of a broad range of transgenic animals using systems similar to the claimed invention. Thus, these references demonstrate that making transgenic animals in general was routine at the time the application for the claimed invention was filed.

For at least these reasons, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

II. Claim Rejections – 35 U.S.C. § 112, Second Paragraph

Claims 21, 24-27, and 29-32 stand rejected under 35 U.S.C. § 112, second paragraph, because the examiner argues that the term “detectable levels” “is a relative word and the metes and bounds of the term cannot be determined and therefor is not clear.” Applicants respectfully traverse this ground of rejection.

The term “detectable levels” is clear and definite to one of skill in the art. A rejection under 35 U.S.C. § 112, second paragraph, is improper if the basis of the rejection is merely because the claim could be made more clear. MPEP § 2173.02. Instead, an indefiniteness rejection is only proper when one of skill in the art could not interpret the metes and bounds of a claim. *Id.* Here, one of skill in the art could readily understand the metes and bounds of the claim in light of the specification. Indeed, the specification discloses enzyme linked immunosorbent assays (ELISA) as one method for monitoring the expression of the regulated protein. A skilled artisan would clearly understand the limits of ELISA and be able to determine what constitutes a “detectable level[.]” In addition, the specification discloses a method for detecting expression employing a detectable marker (page 25, lines 22-25). One of skill in the art would be able to select a suitable assay depending on the particular application. Accordingly, “detectable levels” is clear and definite, because one of skill in the art would understand what constitutes “detectable levels” depending on the particular application. For at least these reasons, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

III. Claim Rejections – Double Patenting

Claims 21, 24-27, and 29-54 stand rejected under the judicially created doctrine of obviousness-type double patenting as being allegedly unpatentable over claims 1-36 of U.S. Patent No. 5,912,411. Claims 22, 23, and 28 stand rejected under the judicially created doctrine

of obviousness-type double patenting as being unpatentable over claims 1-36 of U.S. Patent No. 5,866,755.

Applicants will address these issues upon the claims being found otherwise allowable.

CONCLUSION

The present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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By 

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